# SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## I. GENERAL INFORMATION

Device Generic Name: Pulse Generator (PG), Implantable Pacemaker
Lead: Steroid-eluting, endocardial, bipolar, pace/sense lead

Device Trade Name: St. Jude Medical MR Conditional Pacemaker System, consisting of:

- Assurity MRI™ Models PM 1272, PM 2272
- Endurity MRI™ Models PM 1172, PM 2172
- Tendril MRI™ Lead Model LPA 1200M
- MRI Activator™ Model EX4000
- Merlin™ PCS Programmer Software Model 3330 v 22.1.1
- Merlin.net MN5000 7.4d
- Merlin@home EX2000 8.2.2

Device Procode: LWP
NVN

Applicant's Name and Address: St. Jude Medical
15900 Valley View Court
Sylmar, CA 91342

Date of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P140033

Date of FDA Notice of Approval: January 31, 2017

## II. INDICATIONS FOR USE

**Assurity MRI™ Model PM1272 and Model 2272 and Endurity MRI™ Models PM1172 and Model 2172 pacemakers**

Implantation of a single-chamber pulse generator or dual-chamber pulse generator is indicated in one or more of the following permanent conditions:

- Syncope
- Presyncope
- Fatigue
- Disorientation
- Or any combination of those symptoms.

**MR Conditional** pacemakers are conditionally safe for use in the MRI environment when used in a complete MR Conditional system and according to the instructions in the MRI procedure document for the St. Jude Medical MR Conditional System.

**Rate-Modulated Pacing** is indicated for patients with chronotropic incompetence, and for those who would benefit from increased stimulation rates concurrent with physical activity. Chronotropic incompetence has not been rigorously defined. A conservative approach, supported by the literature, defines chronotropic incompetence as the failure to achieve an intrinsic heart rate of 70% of the age-predicted maximum heart rate or 120 bpm during exercise testing, whichever is less, where the age-predicted heart rate is calculated as 197 – (0.56 x age).

**Dual-Chamber Pacing** (Dual-chamber pulse generators) is indicated for those patients exhibiting:

- Sick sinus syndrome
- Chronic, symptomatic second- and third-degree AV block
- Recurrent Adams-Stokes syndrome
- Symptomatic bilateral bundle branch block when tachyarrhythmia and other causes have been ruled out.

**Atrial Pacing** is indicated for patients with sinus node dysfunction and normal AV and intraventricular conduction systems.

**Ventricular Pacing** is indicated for patients with significant bradycardia and:

- Normal sinus rhythm with only rare episodes of A-V block or sinus arrest
- Chronic atrial fibrillation
- Severe physical disability

**AF Suppression** (Dual-chamber pulse generators) is indicated for suppression of paroxysmal or persistent atrial fibrillation episodes in patients with one or more of the above pacing indications.

**Tendril MRI™ Model LPA1200M Lead**
The Tendril MRI lead is a 7.9 French, transvenous, steroid eluting, bipolar, IS-1 compliant active fixation lead designed for permanent sensing and pacing in either the right atrium or the right ventricle, in combination with a compatible device. Active leads such as the Tendril MRI lead may be indicated for patients where permanent fixation of passive fixation leads is suspected to be unstable.

In atrial applications, the use of screw-in leads such as Tendril MRI lead may be indicated in the presence of an abnormal, surgically altered or excised atrial appendage.

**SJM MRI Activator™ Model EX4000 handheld device**
The MRI Activator handheld device is used to evaluate the status of, and to enable and disable, the previously stored MRI settings. The activator is intended for use with St. Jude Medical MR Conditional pulse generators.

## III. CONTRAINDICATIONS

**Assurity MRI and Endurity MRI**
Single-chamber pulse generators, dual-chamber pulse generators, and CRT-Ps are contraindicated in patients with an implanted cardioverter-defibrillator.

Rate-Adaptive Pacing may be inappropriate for patients who experience angina or other symptoms of myocardial dysfunction at higher sensor-driven rates. An appropriate Maximum Sensor Rate should be selected based on assessment of the highest stimulation rate tolerated by the patient.

AF Suppression (Dual-chamber pulse generators) stimulation is not recommended in patients who cannot tolerate high atrial-rate stimulation.

Dual-Chamber Pacing (Dual-chamber pulse generators), though not contraindicated for patients with chronic atrial flutter, chronic atrial fibrillation, or silent atria, may provide no benefit beyond that of single-chamber pacing in such patients.

Single-Chamber Ventricular Demand Pacing is relatively contraindicated in patients who have demonstrated pacemaker syndrome, have retrograde VA conduction, or suffer a drop in arterial blood pressure with the onset of ventricular pacing.

Single-Chamber Atrial Pacing is relatively contraindicated in patients who have demonstrated compromise of AV conduction.

**Tendril MRI**
The Tendril MRI lead is contraindicated:

- in the presence of tricuspid atresia
- for patients with mechanical tricuspid valves
- in patients who are expected to be hypersensitive to a single dose of one milligram of dexamethasone sodium phosphate

**SJM MRI Activator**
There are no known contraindications for the SJM MRI Activator handheld device.

**MRI Procedure**

- Patient has elevated body temperature or compromised thermoregulation at time of scan.
- The device is at End-of-Life
- A combination of lead(s) and device that is not listed as MR Conditional in the device/lead combinations table
- Broken or intermittently functioning St. Jude Medical MR Conditional leads
- Lead impedance measurements not within the programmed lead impedance limits
- Abandoned cardiac hardware, including leads, lead extenders, or lead adaptors

- A St. Jude Medical MR Conditional system implanted in sites other than the left and right pectoral region (see figure below)
- Unstable capture thresholds or capture threshold values of > 2.5 V at a pulse width of 0.5 ms
- Complaints of diaphragmatic stimulation at a pacing output of 5.0 V or 7.5 V and at a pulse width of 1.0 ms in patients whose device will be programmed to an asynchronous pacing mode when MRI Settings are enabled

## IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Assurity MRI™ Model PM1272 and Model 2272 and Endurity MRI™ Models PM1172 and Model 2172 pacemakers, Tendril MRI™ Model LPA1200M lead, and the SJM MRI Activator™ Model EX4000 handheld device respective labeling.

## V. MRI CONDITIONS OF USE

Based on its use as a system versus an individual device, specific procedures and restrictions apply to magnetic resonance imaging (MRI) scans in patients with the MR Conditional Pacemaker System. When used as a system and according to the instructions provided in the MRI-Ready Systems Manual, the MR Conditional Pacemaker System has been determined to meet the status of Magnetic Resonance (MR) Conditionally safe.

Physicians and Clinicans are instructed to perform the following steps. Each item is further elaborated in the MRI-Ready Systems Manual.

- Confirm that the patient has an MR Conditional system
- Confirm that no conditions adverse to MRI scanning are present
- Review the potential adverse events
- Generate a report of the patient's permanently programmed parameters
- Select and Save MRI Settings
- Review the MRI Checklist and Program the MRI Settings
- Disable the MRI Settings

Radiologists and MRI Technologists are instructed to perform the following steps. Each item is further elaborated in the MRI-Ready Systems Manual.

- Confirm that the patient has an MR Conditional system
- Confirm that no conditions adverse to MRI scanning are present
- Review the potential interactions between the MRI scanner and the MR Conditional system
- Select the Correct Scan Parameters
- Check the MRI Settings status
- Perform the Scan and Monitor the Patient
- Disable the MRI Settings

The scan parameters for the MR Conditional Pacemaker System are detailed in the table below.

| Scan Parameters | Setting |
|---|---|
| Scanner Type | Cylindrical-bone magnet, horizontal field orientation |
| Magnet Strength | 1.5 Tesla/64 MHz excitation frequency (hydrogen atom) |
| Spatial Field Gradient | ≤30 T/m (3000 G/cm) |
| MR Operating Mode | Normal Operation Mode |
| Whole Body SAR (Specific Absorption Rate) | ≤2 W/kg |
| Head SAR | ≤3.2 W/kg |
| Gradient Slew Rate | ≤200 T/m/s |
| Scan Regions | Full Body |

## VI. DEVICE DESCRIPTION

**Assurity MRI™ Model PM1272 and Model 2272 and Endurity MRI™ Models PM1172 and Model 2172 pacemakers**

The Assurity MRI and Endurity MRI pacemakers are based on the market approved Assurity and Endurity pacemakers. All commercially available features of the market approved pacemakers are included in the MRI devices.

The MRI pacemakers have new hardware and firmware to prevent unintended stimulation due to electromagnetic fields created by the MRI scanner. The new hardware and firmware include:

- Reduction in feed-through capacitance to mitigate gradient induced stimulation.
- Addition of a band-stop filter (MR filter assembly) to limit the ingress of MRI-specific frequencies which otherwise could result in RF rectification and/or interference.
- The device shape and size was modified to accommodate the MRI filter assembly. The MRI pacemakers also have an unique MRI radiopaque x-ray marker.

Due to the noise created by the MRI environment, sensing must be disabled for the duration of an MRI scan. Therefore, firmware and programmer software will include the capability to program the device to MRI conditionally safe settings. The MRI Mode will provide the physician with two (2) options: either asynchronous pacing or pacing off. The MRI Setting consists of nonprogrammable and programmable pacing parameters. The Merlin™ PCS programmer software will include:

- Ability for the user to pre-set the MRI parameters in advance and save these in the device as an “MRI Setting”.
- Checklist feature allowing the user to confirm that the system meets all conditions required for safe MRI scanning.
- Capability to program the device into MRI Setting, out of MRI Setting, and back into the previously programmed settings.

- Ability to set an MRI Ready status in the device for future use with the MRI Activator.
- Collection of diagnostics from the MRI Setting (time in MRI setting, etc.) and display via MRI-related reports.

The devices are supported on the Merlin PCS Programmer Software Model 3330 v22.1.1.

**Tendril MRI™ LPA 1200M Lead**
The Tendril MRI lead is an endocardial, bipolar, active fixation lead with an IS-1 connector based on the currently marketed Tendril™ Model 1888TC lead. The Tendril MRI lead incorporates a filter to mitigate MRI induced radiofrequency (RF) tissue heating near the lead electrodes. It has a radiopaque identification marker built into the connector end allowing the physician to identify the lead as MRI compatible via x-ray. The lead's body has a co-axial design and uses MP35N coils and an Optim outer insulation. The lead has been designed to fit through an 8F introducer without a retained guide wire.

**MRI Activator™ EX4000**
The external MRI Activator is a handheld device that allows the user to enable or disable the MRI Setting in the MRI pacemakers if the checklist conditions have been verified and the use of the MRI Activator has been approved and enabled by the physician. The MRI Activator hardware is based on the commercially available Confirm™ Patient Activator hardware (K081365). The MRI Activator firmware will include the capability to program the MRI Setting on and off, and back into the previously programmed settings if the pacemaker has been made MRI ready.

## VII. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for rate adaptive pacing and chronic cardiac pacing. Alternative therapies include the use of other commercially available dual or single chamber rate adaptive pacing systems that are labeled as MR Conditional. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

## VIII. MARKETING HISTORY

The Assurity MRI and Endurity MRI pacemakers, the Tendril MRI lead, and the MRI Activator (the SJM Brady MRI System) are currently distributed commercially outside the United States. Specifically, the SJM Brady MRI System is market approved in the European Community, Japan, Korea, and Latin America.

Neither the pacemakers nor the lead have been withdrawn from the market in any country for any reason related to safety and effectiveness.

## IX. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below are a list of the potential adverse effects (e.g., complications) that may occur with the use of the pacing system or transvenous leads or as a result of the interaction between the investigational pacing system and the MRI system that occurs during the MRI scan.

- **Potential MRI System Adverse Events**
  - Lead electrode heating and tissue damage resulting in loss of sensing or capture or both
  - Lead heating resulting in thrombus formation or embolism
  - Pulmonary embolism
  - Device heating resulting in tissue damage in the implant pocket or patient discomfort or both
  - Induced currents on leads resulting in continuous capture, VT/VF, Hemodynamic collapse, or all three (3)
  - Damage to the device or leads causing:
    - the system to fail to detect or treat irregular heartbeats
    - the system to treat the patient's condition incorrectly
    - damage to the functionality or mechanical integrity of the device resulting in the inability of the device to communicate with the programmer
  - Movement or vibration of the device or leads
  - Lead dislodgement
  - Competitve pacing and potiential for VT/VF induction if asynchronous pacing is programmed when MRI Settings are enabled
  - Syncope due to loss of pacing if no pacing support is programmed with MRI settings
  - Death due to untreated spontaneous arrhythmis because tachy therapy is disabled when MRI settings are programmed.

- **Potential Pacing System Adverse Events**
  - Air embolism
  - Body rejection phenomena
  - Cardiac tamponade or perforation
  - Hematoma, bleeding hematoma, seroma
  - Formation of fibrotic tissue; local tissue reaction
  - Inability to interrogate or program due to programmer or device malfunction
  - Infection/erosion
  - Interruption of desired pulse generator function due to electrical interference either electromyogenic or electromagnetic
  - Loss of capture or sensing due to lead dislodgement or reaction at the electrode/tissue interface
  - Loss of desired pacing and/or sensing due to lead displacement, body reaction at electrode interface, or lead malfunction (fracture or damage to insulation)
  - Lead malfunction due to conductor fracture or insulation degradation

- Loss of normal pacemaker function due to battery failure or component malfunction
- Pacemaker migration, pocket erosion
- Pectoral muscle stimulation
- Phrenic nerve or diaphragmatic stimulation
- Pneumothorax/hemothorax
- Endocarditis
- Excessive bleeding
- Induced atrial or ventricular arrhythmias
- Myocardial irritability
- Pericardial effusion
- Pericardial rub
- Pulmonary edema
- Rise in threshold and exit block
- Valve damage

- **Potential lead related adverse events**
  - Cardiac tamponade
  - Diaphragmatic/phrenic nerve stimulation
  - Embolism
  - Excessive bleeding
  - Induced ventricular ectopy
  - Infection
  - Loss of pacing and/or sensing due to dislodgement or mechanical malfunction of the pacing lead
  - Thrombosis

For specific adverse events that occurred in the clinical study, please see Section XI - Summary of Clinical Study.

## X. SUMMARY OF NONCLINICAL STUDIES

Extensive preclinical MRI testing was done to assess the safety and effectiveness of the St. Jude Medical MR Conditional Pacemaker System. The performance of the pacemaker system was examined when exposed to the static magnetic, radiofrequency, and gradient magnetic fields in a bench testing environment to ensure the system was not influenced by these fields (individually or combined).

Pre-Clinical test methods included in vitro (bench) testing, in vivo (animal) testing, and computer simulations (modeling).

## A. Laboratory Studies

**MRI Environment Testing**

**Verification and Validation Testing- MRI Safety**

Preclinical testing of the SJM Brady MRI System, presented in **Table1** below, includes MRI related hazards and associated tests. "Pass" as used below denotes that the device met established performance criteria and/or specifications or was in conformance with the requirements of the standard to which it was tested.

**Table 1: MRI Environment Testing Summary**

| General Hazards to the Patient | Test Requirement | SJM MRI Proof of Safety Evaluation / Test Name | Acceptance Criteria | Result (Pass/Fail) |
|---|---|---|---|---|
| Heat | RF field-induced heating of the AIMD | Heat – RF | On exposure of the MR Conditional System to RF fields, when scanned under the defined MRI Conditions, the system shall ensure that:<br>The 90$^{th}$ percentile heating is less than or equal to:<br>• 43 °C for myocardial tissue after 30 minutes exposure<br>The 99$^{th}$ percentile heating is less than or equal to:<br>• 45 °C for myocardial tissue after 30 minutes exposure<br>The 99.9$^{th}$ percentile heating is less than or equal to:<br>• 50 °C for blood<br>The 99$^{th}$ percentile heating is less than or equal to:<br>• 44 °C for pocket tissue after 30 minutes exposure assuming a starting temperature of 35 °C | Pass<br>Pass |
| | Gradient field-induced device heating | Heat – Gradient | For exposure of the MR Conditional System to 56 T/s (rms) gradient fields, the device shall ensure that:<br>-The maximum resultant | Pass |

| General Hazards to the Patient | Test Requirement | SJM MRI Proof of Safety Evaluation / Test Name | Acceptance Criteria | Result (Pass/Fail) |
|---|---|---|---|---|
| | | | heating is less than or equal to:<br>• 44 °C for pocket tissue after 30 minutes exposure, assuming a starting temperature of 35 °C. | |
| Vibration | Gradient field-induced vibration | Vibration – Device Damage | For vibrations induced by the MR environment, the MR Conditional System shall deliver pacing output per programmed MRI Settings during exposure and operate per specifications after exposure. | Pass |
| | | Vibration – Patient Harm | The MR Conditional device shall have a maximum vibration value of $5 m/s^2$ (weighted RMS) based on an extremity daily 8-hour occupational exposure, per Human Vibration Directive 2002/44/EC. | Pass |
| Force | $B_0$-induced force | Force | The maximum pressure and stress exerted by the static magnetic force on the MR Conditional pulse generator shall be less than or equal to 10 kPa for pressure exerted on the pocket tissue and 1 MPa for stress exerted on the pocket tissue. | Pass |
| Torque | $B_0$-induced torque | Torque | The maximum torque induced by the static magnetic field shall be less than the gravity torque, defined as the product of the maximum linear dimension of the pacemaker and its weight. | Pass |
| Gradient-induced | Gradient field-induced lead | Pulse Generation – | The MR Conditional Pacing System shall prevent the | Pass |

| General Hazards to the Patient | Test Requirement | SJM MRI Proof of Safety Evaluation / Test Name | Acceptance Criteria | Result (Pass/Fail) |
|---|---|---|---|---|
| Extrinsic Electric Potential | voltage | Gradient | slewing of gradient magnetic fields, defined under the conditions of the MRI Procedure, from inducing voltages on the pacing system by ensuring that the probability of the charge generated above 69 nC is less than 1 in $10^5$. | |
| | | Pulse Cancellation – Gradient | The MR Conditional system shall ensure that the intended delivered charge is not reduced by more than 50% due to gradient induced currents. | Pass |
| | | | The system shall continue to provide bradycardia support with no pause longer than three seconds during combined MRI field exposure, under the conditions defined by the MRI Conditions. | Pass |
| | | Rectification – Gradient | Gradient-induced, rectified current shall be less than 75 μA (which is to say the probability of stimulation from gradient-rectified current is less than 1 in $10^5$). | Pass |
| | $B_0$ static, gradient, and RF | Pulse Cancellation – Combined Fields | The system shall continue to provide bradycardia support with no pause longer than three seconds during combined MRI field exposure, under the conditions defined by the MRI Conditions. | Pass |
| | | | The MR Conditional system shall ensure that the pacing pulse amplitude is >= 2.5 V due to combined fields during MRI scanning. | Pass |

| General Hazards to the Patient | Test Requirement | SJM MRI Proof of Safety Evaluation / Test Name | Acceptance Criteria | Result (Pass/Fail) |
|---|---|---|---|---|
| RF - Rectification | RF field-induced rectified lead voltage | Rectification – RF | RF-Induced, rectified current shall be less than 75 μA (which is to say the probability of stimulation from RF-rectified current is less than 1 in $10^5$). | Pass |
| Malfunction | RF field-induced device malfunction | Damage – RF (Injected) | The MR Conditional System shall ensure that the intended delivered charge is not reduced by more than 50% due to RF-induced currents. | Pass |
| | | | The DUT shall operate within its specifications following exposure to the MR environment under the conditions defined by the MRI procedure. | Pass |
| | | Damage – RF (Radiated) | The DUT shall operate within its specifications following exposure to the MR environment under the conditions defined by the MRI procedure. | Pass |
| | Gradient field-induced device malfunction | Damage – Gradient (Injected) | The MR Conditional system shall ensure that the intended delivered charge is not reduced by more than 50% due to gradient induced currents. | Pass |
| | | | The DUT shall operate within its specifications following exposure to the MR environment under the conditions defined by the MRI procedure. | Pass |
| | | Damage – Gradient (Radiated) | The DUT shall operate within its specifications following exposure to the MR environment under the conditions defined by the MRI | Pass |

| General Hazards to the Patient | Test Requirement | SJM MRI Proof of Safety Evaluation / Test Name | Acceptance Criteria | Result (Pass/Fail) |
|---|---|---|---|---|
| | | | procedure. | |
| | $B_0$ field-induced device malfunction | Damage – Magnet | The DUT shall operate within its specifications following exposure to the MR environment under the conditions defined by the MRI procedure. | Pass |
| | $B_0$ static, gradient, and RF | Damage – Combined Fields | The DUT shall operate within its specifications following exposure to the MR environment under the conditions defined by the MRI procedure. | Pass |

**Bench Testing (outside MRI Environment) - Assurity MRI/Endurity MRI Pacemaker**

**Biocompatibility**
The materials used in the Assurity MRI/Endurity MRI pacemakers that are directly exposed to body tissue and/or fluids are titanium, hysol high purity epoxy, silicone septum, and septum adhesive. These materials have all been used in St Jude Medical pacemakers (Assurity /Endurity approved on March 4, 2014 under PMA P880086/S230). No new materials or processes were introduced with the Assurity MRI/Endurity MRI pacemakers that would introduce new issues of biocompatibility.

**Package Testing**
The packaging process including sealing parameters and materials of the Assurity MRI/Endurity MRI pacemakers is identical to the packaging of the legally marketed Assurity/Endurity pacemakers. Therefore, re-verification of the heat sealing process was not deemed necessary.

**Sterilization**
The sterilization process of the Assurity MRI/Endurity MRI pacemakers is identical to the sterilization process of other SJM legally marketed low voltage family of pulse generators including Assurity/Endurity pacemakers utilizing 100% Ethylene Oxide. Routine validation of the sterilization equipment is performed in accordance with the Association for the Advancement of Medical Instrumentation, Medical Device Validation and routine control of ethylene oxide sterilization (ANSI/AAMI/ISO 11135:2007).

**Shelf Life**
Shelf life of the Assurity MRI/Endurity MRI pacemakers is limited by the battery and is 18 months, the same as other SJM market approved pacemakers.

**Mechanical and Electrical Testing**
The Assurity MRI/Endurity MRI pacemakers is based on previously FDA approved pacemaker hardware platform (P880086/S230, approved March 20, 2014) with enhancements focused primarily on making the device safe in a MR environment under specified conditions. The only hardware changes include:

- New MRI filter board comprising of feed-thru assembly and passive components such as inductors and capacitors to mitigate against RF rectification and/or other interference
- Updated X-ray ID tag

Verification activities were carried out to ensure these changes met acceptance criteria. Several of the Assurity MRI/Endurity MRI pacemaker components are equivalent to those of the previously approved Assurity/Endurity pacemakers therefore verification and verification by similarity activities were performed according to specifications. All components used in the Assurity MRI/Endurity MRI pacemakers were determined to have acceptable quality and reliability.

Standard mechanical and electrical verification testing were performed. These included: EMC testing, EMI testing, Electrical Design Verification Testing, and Mechanical Design Verification Testing. All evaluations were successfully completed demonstrating the electrical and mechanical testing meets its requirements. The main verification tests that were performed are as follows:

| Test Procedure | Acceptance Criteria | Result |
|---|---|---|
| X-Ray ID Verification | The x-ray ID tag shall be visible on the screen. | Pass |
| Marking Evaluation | Per ISO 14708-2:2012 and EN45502-2-1 Clause 13.1.1. The Artwork shall contain:<br>1. St Jude Medical Name or Trademark<br>2. Model Number of device<br>3. Location to place serial number of device<br>4. The most comprehensive pacing mode<br>a. Single Chamber Devices: SSIR<br>b. Dual Chamber Devices: DDDR<br>5. For dual chamber devices:<br>a. The ventricular terminal shall be marked with the symbolic designation “V”<br>b. The atrial terminal shall be marked with the symbolic designation “A” | Pass |

| Test Procedure | Acceptance Criteria | Result |
|---|---|---|
| Pressure Test | The device shall provide uninterrupted pacing during exposure. Permanent deformation of the implantable device is acceptable as long as there are no sharp edges. The device shall pass the ATE test requirements. | Pass |
| Pacing Pulse Amplitude | For testing per EN 45502-2-1 and ISO14708-2, the atrial and ventricular pulse amplitude of the device shall be documented in the test report.<br>For testing per 60058978, the measured atrial and ventricular pulse amplitude shall be ± 20% of the programmed pulse amplitude at BOL. | Pass |
| Pacing Pulse Duration | For testing per ISO 14708-2; the measured atrial and ventricular pulse width of the device shall be documented in the test report. | Pass |
| Pacing Pulse Interval and Pulse Rate | For testing per ISO 14708-2; the measured atrial and ventricular pacing interval of the device shall be documented in the test report. | Pass |
| Atrial/Ventricular Sensitivity Threshold | For testing per 60058978, the measured atrial sensitivity threshold shall be within ± 30% of the programmed atrial sensitivity.<br>For testing per 60058978, the measured ventricular sensitivity shall be within ±30% or 0.3 mV of the programmed ventricular sensitivity, whichever is greater.<br>For testing per EN 45502-2-1 and ISO14708-2, the measured atrial and ventricular sensitivity threshold of the device shall be documented in the test report. | Pass |
| A-V Interval After Sensing (P-V Delay) | For testing per 60058978, the measured A-V Interval after Sensing (P-V Delay) shall be ± 10 ms of the programmed Sensed AV Delay.<br>For testing per EN 45502-2-1 and ISO14708-2, the measured A-V Interval after Sensing (P-V Delay) of the device shall be documented in the test report. | Pass |
| Post Ventricular Atrial Refractory Period (PVARP) | For testing per 60058978, the measured post ventricular atrial refractory period (PVARP) shall be ± 10 ms of the programmed PVARP.<br>For testing per EN 45502-2-1 and ISO14708-2, the measured post ventricular atrial refractory period (PVARP) of the device shall be documented in the test report. | Pass |
| Escape Interval | For testing per 60058978, the measured Escape Interval shall be ± 15 ms of the programmed pulse interval.<br>For testing per EN 45502-2-1 and ISO14708-2, the measured Escape Interval of the device shall be documented in the test report. | Pass |

| Test Procedure | Acceptance Criteria | Result |
|---|---|---|
| Pacing Refractory Period | For testing per 60058978, the measured atrial and ventricular Pacing Refractory Period shall be ± 10 ms of the programmed atrial Pacing Refractory Period.<br>For testing per EN 45502-2-1 and ISO14708-2, the measured atrial and ventricular Pacing Refractory Period of the device shall be documented in the test report. | Pass |
| Sensing Refractory Period | For testing per 60058978, the measured atrial and ventricular Sensing Refractory Period shall be ± 5 ms of the programmed atrial Sensing Refractory Period.<br>For testing per EN 45502-2-1 and ISO14708-2, the measured atrial and ventricular Sensing Refractory Period of the device shall be documented in the test report. | Pass |
| Pacing Lead Impedance (PLI) | For testing per 60058978, the atrial and ventricular pacing lead impedance shall meet the following requirements:<br>• Pacing Lead Impedance: ± 20% (200 - 2000 ohms)<br>• Pacing Lead Impedance: ± 30% (>2000 - 3000 ohms)<br>• Pacing Lead Impedance: ± 30% (100 - <200 ohms) | Pass |
| Pacing Capacitance | For testing per ISO14708-2, the Pacing Capacitance of the device shall be documented in the test report. | Pass |
| Input Impedance | For testing per EN 45502-2-1 and ISO14708-2, the Input Impedance of the device shall be documented in the test report. | Pass |
| Backup Atrial/Ventricular Sensitivity Threshold | For testing per 60058978, the measured Backup ventricular sensitivity threshold shall be within 2 mV ± 30%. | Pass |
| Backup Pacing Pulse Amplitude | For testing per 60058978, the measured Backup Pacing Pulse Amplitude peak shall be 5 V ± 20 % (BOL to ERI). | Pass |

<table>
<tr><th>Test Procedure</th><th>Acceptance Criteria</th><th>Result</th></tr>
<tr><td>Induced Lead Current</td><td>Per EN45502-2-1 clause 27.2 and ISO14117 clause 4.2.2, the measured induced current shall meet the requirements listed below:<br><br><u>For test voltage 1:</u><br><br><table><tr><th colspan="2">Injection Current Limits for Sense/Pace Terminals</th></tr><tr><th>Magnitude</th><th>Frequency</th></tr><tr><td>50 μA RMS</td><td>16.6 Hz ≤ f ≤ 1 kHz</td></tr><tr><td>50 μA * f/1 kHz RMS</td><td>1 kHz ≤ f ≤ 20 kHz</td></tr></table><br><u>For test voltage 2:</u><br>The current measurement at 130 Hz shall be less than or equal to 50 μA RMS.</td><td>Pass</td></tr>
<tr><td>Protection from persisting malfunction attributable to ambient electromagnetic fields</td><td>Per EN45502-2-1 clause 27.3 and ISO14117 clause 4.3.2, compliance shall be met if, after application of the specified test signals, the device functions as prior to the tests without further adjustment. The device shall pass the ATE test requirements.</td><td>Pass</td></tr>
</table>

| Test Procedure | Acceptance Criteria | Result |
|---|---|---|
| Temporary response to continuous wave sources | Based on EN45502-2-1 clause 27.4 and ISO14117 clause 4.4.1:<br>• Compliance shall be confirmed if while the test conditions are varied as required, the test device continues to operate as set or in its interference mode (Noise mode) as follows:<br>o The Atrial Noise mode is "Pacing off" for frequencies below approximately 30Hz and "Fixed rate pacing" for frequencies above approximately 30Hz.<br>o The Ventricular Noise Mode is "Fixed rate pacing" for the frequency range of 16.6Hz to 167kHz.<br>• If for some value of the test conditions, the test device changes from its set mode to its interference mode (Noise mode), or vice versa, then no pause longer than twice the pre-set interval shall occur unless the change of mode is completed within a change by a factor of two in voltage of the test signal.<br>• For those sensing threshold settings of the test device for which the conformity cannot be achieved, compliance shall be confirmed if an appropriate warning is provided in the accompanying documentation per ISO14117 clause 7.1 | Pass |
| Protection from sensing EMI as cardiac signals in the 16.6Hz-150kHz frequency range | Based on EN45502-2-1 clause 27.5.1 and ISO14117 clause 4.5.2.1:<br>• Compliance for the sensing thresholds tested shall be confirmed if the test device at all times functions in its set mode, both with and without the simulated heart signal applied by the inhibition signal generator and irrespective of the application of the required test signal.<br>For those sensing threshold settings of the test device for frequencies up to 1 kHz, at which a change of pattern occurs, compliance shall be confirmed if an appropriate warning and disclosure is provided in the accompanying documentation per EN45502-2-1 clause 28.22.1 and ISO14117 clause 7.1. | Pass |
| Protection from sensing EMI as cardiac signal in the 150 kHz- 10 MHz frequency range | Per EN45502-2-1 clause 27.5.2 and ISO14117 clause 4.5.3.1, compliance for the sensing thresholds being tested shall be confirmed if the test device at all times functions in its set mode irrespective of the application of the required modulated signal. | Pass |

| Test Procedure | Acceptance Criteria | Result |
|---|---|---|
| Protection from sensing modulated EMI as cardiac signals in the 10 MHz – 450 MHz frequency range | Per EN45502-2-1 clause 27.5.3 and ISO14117 clause 4.5.4.1, compliance for the sensing thresholds being tested shall be confirmed if the test device at all times functions in its set mode irrespective of the application of the required modulated signal. | Pass |
| Protection from static magnetic fields of flux density up to 1 mT | Per EN45502-2-1 clause 27.6 and ISO14117 clause 4.6.2, compliance shall be confirmed if the pacemaker remains inhibited while the magnetic field is applied. | Pass |
| Protection from static magnetic fields of flux density up to 50 mT | Per ISO14117 clause 4.7.2, compliance shall be met if, after application of the specified test signals, the test device functions as prior to the tests without further adjustment. The device shall pass the ATE test requirements. | Pass |
| Protection from AC magnetic field exposure in the range of 1 kHz to 140 kHz | Per EN45502-2-1 clause 27.8 and ISO14117 clause 4.8.2, compliance shall be met if, after application of the specified test signals, the test device functions as prior to the tests without further adjustment. The device shall pass the ATE test requirements. | Pass |
| Test requirements for the frequency range of 450 MHz ≤f ≤ 3000 MHz | Per ISO14117 clause 4.9, compliance shall be met if:<br>a) With simulated heart signal off:<br>During test exposure with the simulated heart signal off, the test device shall not exhibit any deviation in pace-to-pace interval that exceeds 10 % of the programmed rate.<br>At the completion of the testing, or immediately prior to any reprogramming during test, the programmed parameters shall be unaltered from pre-exposure values.<br>b) Simulated heart signal on.<br>During test exposure with the simulated heart signal on, the test device shall not exhibit any pace pulses during application of ECG and RF signals.<br>At the completion of the testing, or immediately prior to any reprogramming during test, the programmed parameters shall be unaltered from pre-exposure values.<br>Per ISO14117 clause 4.3.2.3, compliance shall be confirmed if the test device functions as it did before the test without further adjustment. The device shall pass the ATE test requirements. | Pass |

**Firmware Testing**
Assurity MRI/Endurity MRI firmware verification testing was carried out according to the software verification plan for device firmware, which was created to ensure that the firmware meets its requirements as defined in the device requirement specification. These verification activities were carried out and the results demonstrate that the system requirements have been met.

**Software Testing**
Verification testing of all software requirements was conducted in accordance with the software verification plan developed to ensure that the Assurity MRI/Endurity MRI pacemakers software was tested to its specified requirements. The Model 22.1.1 software application met its requirements.

**Bench Testing (outside MRI Environment) - Tendril MRI LPA 1200M Lead**

**Biocompatibility**
The materials used in the Tendril MRI pacing lead that are directly exposed to body tissue and/or fluids are titanium nitride coated platinum iridium, platinum iridium, titanium, MP35N with blue ETFE coating, silicone rubber, PEEK Optima LT3, clear polyester tubing, Optim, polyvinylpyrrolidone, and stainless steel. Materials are either identical to materials used in previously approved SJM products (P960013/S006, S007, S013, S015, S018, S057 and P950022/S040, S041) or new materials which have not been used in SJM devices previously. Cytotoxicity, sensitization, intracutaneous reactivity, acute systemic toxicity, subchronic toxicity, implantation, genotoxicity, and haemocompatibilty testing has been performed to assess the Tendril MRI pacing lead with acceptable results.

**Packaging Testing**
There is no change to the Tendril MRI pacing lead packaging process or materials and continues to be in a double PETG tray with Tyvek lid. Therefore, no additional testing was deemed necessary.

**Sterilization**
The sterilization of the Tendril MRI pacing lead is the same as of other SJM legally marketed family of leads. The Tendril MRI leads sterilization was adopted into the currently approved 100% EO sterilization Cycle 100. Testing was conducted to ensure that the Tendril MRI lead meets the EO residual, particulate release, bioburden and bacterial endotoxin requirements with acceptable results.

**Shelf Life**
Shelf Life for the Tendril MRI is currently 6 months based on the real time and accelerated shelf life testing as well as an assessment of the benefit/risk profile of the device.

**Mechanical and Electrical Verification**

Design verification testing was conducted on the Tendril MRI lead to make sure it met its design requirements. The verification activities were conducted under different protocols and included environmental pre-conditioning which consisted of standard sterilization, temperature cycling, temperature shock, and implant handling. The main verification test that were performed is as follows:

| Test Procedure | Acceptance Criteria | Result |
|---|---|---|
| Lead Length | The samples' standard lead length between the tip and the IS-1 pin shall be the following:<br><br>Lead Length (± 0.7 cm)<br>46<br>52<br>58 | Pass |
| Extended Helix Length | When fully extended, the helix electrode shall protrude 1.8+/-0.5mm. | Pass |
| Tip-to-Ring Spacing | The distance between the distal end of the ring electrode and the distal end of the soft tip shall be 10 ± 1 mm. | Pass |
| Soft Tip Diameter | The distal soft tip diameter shall be greater than 8 French (2.7 mm). | Pass |
| Connector Composite Strength | The composite of all load-bearing bonds, welds, and crimps between the connector pin and the distal portion (grip zone) of the connector boot shall withstand a minimum of 3.37 pounds (15N) without separation or breakage, and be within the allowable DC resistance range while the load is applied. | Pass |
| Distal End Composite Strength | The composite of all lead conductors and conductor joints between the helix and the lead body, 2 inches from the distal end of the connector boot, shall withstand a minimum of 2 pounds (9 N) and be within the allowable DC resistance range while the load is applied. | Pass |
| Soft Tip Attachment Strength | The samples shall meet a minimum load of 2 lbs (9N). | Pass |
| Lead Durability | The leads shall not exhibit bond separation, cracks, tears, permanent elongation in excess of 5%.<br><br>The leads shall not exhibit resistance outside of the allowable DC resistance range. | Pass |

| Test Procedure | Acceptance Criteria | Result |
|---|---|---|
| Insulation Integrity | The lead current leakage shall not exceed 2 milliamperes during the time that the voltage is applied. | Pass |
| Stylet Insertion / Extraction | In the straight position, the stylet shall be inserted into and removed from the lead without any binding. Insertion and extraction forces shall not exceed 2N/0.45lbs.<br><br>In the curved position, the lead shall allow full insertion and withdrawal of a straight, Ø0.015 inch ball-tipped stylet, with insertion force less than 1.00 pound (4.45 N) and a withdrawal force less than 0.5 pound (2.23 N). | Pass |
| Suture Sleeve Performance | For the Free Slip inspection, the untied suture sleeve shall not fall freely when the lead is held vertically.<br><br>For the Untied Test, the average sliding force of an untied suture sleeve shall not exceed 0.25lbf (1.1N). | Pass |
| Tip Stiffness Test | The tip pressure of the lead shall not exceed 170 kPa. | Pass |
| Introducer Compatibility | The lead shall pass through the introducer (up to the connector boot) without any binding, resulting in visible damage to the lead. | Pass |
| IS-1 Connector Flex | The lead connector test samples shall withstand connector flex testing per ES1571 (Bell Mouth Flex Test Method) for a minimum of 164,000 (2 x standard requirement) cycles without a change of lead conductor resistance greater than ± 25%. | Pass |
| Lead Body Flex Test | The lead body test sample shall withstand flex testing per ES1571 (Bell Mouth Flex Test Method) for a minimum of 94,000 (2 x standard requirement) cycles without a change in lead conductor resistance greater than ±25%. | Pass |
| Distal Tip Fatigue Test | The lead samples shall survive a minimum of 10,000,000 flex cycles without any indication of tubing breach or bond joint delamination in the lead insulation or lead body joints within the region of flexing per distal visual criteria of 60048263. After completion of the test, the DC resistance of each conductor shall not exceed the allowable resistance range. | Pass |

<table>
<tr><th>Test Procedure</th><th>Acceptance Criteria</th><th>Result</th></tr>
<tr><td>Helix Extension Retraction</td><td>In a straight position, the lead shall meet the requirements in the table below for the maximum number of turns to fully extend and retract the helix with either a straight or J-stylet.<br><br><table><tr><td colspan="4">Maximum Number of Turns to Fully Extend and Retract the Helix Electrode</td></tr><tr><td colspan="2">Straight Stylet</td><td colspan="2">J-Stylet</td></tr><tr><td>Extension</td><td>Retraction</td><td>Extension</td><td>Retraction</td></tr><tr><td>11</td><td>13</td><td>11</td><td>13</td></tr></table><br>In a curved fixture, the lead shall meet the requirements in the table below for the maximum number of turns to fully extend and retract the helix with either a straight or J-stylet.<br><br><table><tr><td colspan="4">Maximum Number of Turns to Fully Extend and Retract the Helix Electrode</td></tr><tr><td colspan="2">Straight Stylet</td><td colspan="2">J-Stylet</td></tr><tr><td>Extension</td><td>Retraction</td><td>Extension</td><td>Retraction</td></tr><tr><td>12</td><td>14</td><td>13</td><td>15</td></tr></table></td><td>Pass</td></tr>
<tr><td>Helix Multiple Activation</td><td>After fully extending and retracting the helix 10 times in curved fixture HWT9892, the following criteria shall be met. The maximum number of connector pin revolutions to fully extend and retract the helix electrode in the curved fixture HWT9892, after the distal tip of the lead has been soaked for a minimum of 3 hours in 9 g/l saline solution at 37 ± 5°C, shall meet the requirements below.<br><br><table><tr><td colspan="4">Maximum Number of Turns to Fully Extend and Retract the Helix Electrode</td></tr><tr><td colspan="2">Straight Stylet</td><td colspan="2">J-Stylet</td></tr><tr><td>Extension</td><td>Retraction</td><td>Extension</td><td>Retraction</td></tr><tr><td>12</td><td>14</td><td>13</td><td>15</td></tr></table></td><td>Pass</td></tr>
</table>

<table>
<tr><th>Test Procedure</th><th>Acceptance Criteria</th><th>Result</th></tr>
<tr><td>Helix Over-torque Extension/Retraction</td><td>After fully extending the helix and rotating the connector pin an additional 20 revolutions in the direction of helix extension in the curved fixture, HWT9892, the following criteria shall be met. The maximum number of connector pin revolutions to fully extend and retract the helix electrode in the curved fixture HWT9892, after the distal tip of the lead has been soaked for a minimum of 3 hours in 9 g/l saline solution at 37 ± 5°C, shall meet the requirements shown below.<br><br><table><tr><td colspan="4">Maximum Number of Turns to Fully Extend and Retract the Helix Electrode</td></tr><tr><td colspan="2">Straight Stylet</td><td colspan="2">J-Stylet</td></tr><tr><td>Extension</td><td>Retraction</td><td>Extension</td><td>Retraction</td></tr><tr><td>12</td><td>14</td><td>13</td><td>15</td></tr></table></td><td>Pass</td></tr>
<tr><td>Helix Extension Retraction After Saline Soak</td><td>The maximum number of connector pin revolutions to fully extend and retract the helix electrode in the curved fixture HWT9892, after the distal tip of the lead has been soaked for a minimum of 3 hours in 9 g/l saline solution at 37 ± 5°C, shall meet the requirements in the table below.<br><br><table><tr><td colspan="4">Maximum Number of Turns to Fully Extend and Retract the Helix Electrode</td></tr><tr><td colspan="2">Straight Stylet</td><td colspan="2">J-Stylet</td></tr><tr><td>Extension</td><td>Retraction</td><td>Extension</td><td>Retraction</td></tr><tr><td>12</td><td>14</td><td>13</td><td>15</td></tr></table></td><td>Pass</td></tr>
</table>

<table>
<tr><th>Test Procedure</th><th>Acceptance Criteria</th><th>Result</th></tr>
<tr><td>Lead DC Resistance after Helix Performance</td><td>The DC resistance of the lead conductors shall be as follows:<table><tr><th rowspan="2">Length (cm)</th><th colspan="2">DC Resistance (Ω)</th></tr><tr><th>Tip to Connector Pin</th><th>Ring to Connector Pin</th></tr><tr><td>46</td><td>20 ± 5</td><td>46 ± 12</td></tr><tr><td>52</td><td>22 ± 6</td><td>52 ± 13</td></tr><tr><td>58</td><td>24 ± 6</td><td>59 ± 15</td></tr></table></td><td>Pass</td></tr>
<tr><td>Lead Body Torsion</td><td>The outer insulation of the lead body shall withstand torsional buckling in air at 37°C ± 5°C per 60063033 (Lead Body Torsion Test Method) and the torque at which outer insulation torsional buckling occurs must exceed 0.26 ounce-inch (18.72 gram-cm).</td><td>Pass</td></tr>
<tr><td>Lead Body Bending</td><td>The outer insulation of the lead body shall withstand compressive buckling in air at 37°C ± 5°C per 60063036 (Lead Body Bending Test Method) and the bending circumference at which outer insulation compressive buckling occurs must be less than 2.36 inches (60 mm).</td><td>Pass</td></tr>
<tr><td>Lead Implant Handling</td><td>The leads shall not exhibit any bond separation, or visible damage.</td><td>Pass</td></tr>
<tr><td>DC Resistance</td><td>The DC resistance of the lead conductors shall be as follows:<table><tr><th rowspan="2">Length (cm)</th><th colspan="2">DC Resistance (Ω)</th></tr><tr><th>Tip to Connector Pin</th><th>Ring to Connector Pin</th></tr><tr><td>46</td><td>20 ± 5</td><td>46 ± 12</td></tr><tr><td>52</td><td>22 ± 6</td><td>52 ± 13</td></tr><tr><td>58</td><td>24 ± 6</td><td>59 ± 15</td></tr></table></td><td>Pass</td></tr>
<tr><td>Electrical Polarization</td><td>The maximum tip electrode polarization shall not exceed 210 mV in bipolar mode.</td><td>Pass</td></tr>
<tr><td>Dry Insulation Hipot Resistance</td><td>The lead shall not exhibit any insulation breakdown.</td><td>Pass</td></tr>
<tr><td>Sensing Impedance</td><td>The lead bipolar sensing impedance shall be less than 2500 ohms.</td><td>Pass</td></tr>
</table>

| Test Procedure | Acceptance Criteria | Result |
|---|---|---|
| External Defibrillation Protection | The leads shall not exhibit any bond separation, or visible damage. | Pass |
| IS1 Compatibility – Seal Mechanism | The samples shall have at least one sealing ring in each of the two sealing ring zones per ISO 5841-3:2013 (Section 4.2.1.1). | Pass |
| IS-1 Compatibility - Dimensions | The samples shall comply with the IS-1 dimensional requirements. | Pass |
| IS1 Compatibility - Connector Insertion/Withdrawal | The insertion and withdrawal forces shall not exceed 3.147 lbf (14 N). The lead connectors shall remain intact without damage to the bonds, sealing rings, or tubing when visually inspected after insertion & withdrawal. | Pass |
| IS-1 Compatibility - Electrical Impedance Measurement | The tip to ring, ring to reference, and tip to reference impedances shall be a minimum of 50kΩ. | Pass |
| IS-1 Compatibility - Set Screw Deformation | Following application of setscrew forces, the lead connector shall fit into the lead connector GO gauge per Lead Connector Insertion/Withdrawal Test Method 60048732. The insertion force and withdrawal force shall not exceed 3.147 lbs. (14 N). The lead connectors shall remain intact without damage to the bonds, sealing rings, or tubing when visually inspected per 60048423 after insertion & withdrawal. | Pass |
| IS1 Compatibility – Lead Marking | The samples shall be marked with the symbol “IS-1” and letters “BI”. | Pass |
| Steroid Content | The steroid MCRD shall contain less than 1.0 mg of dexamethasone sodium phosphate. | Pass |
| Lead Sterilization Durability | The lead body shall not exhibit any cracking, bond separation, visible insulation degradation, or damage under microscopy inspection. | Pass |
| Lead Temperature Storage | The lead body shall not exhibit any cracking, bond separation, visible insulation degradation, or damage. | Pass |
| Lead Temperature Cycling | The lead body shall not exhibit any cracking, bond separation, visible insulation degradation, or damage under microscopy inspection. | Pass |
| Lead Temperature Shock | The lead body shall not exhibit any cracking, bond separation, visible insulation degradation, or damage under microscopy inspection. | Pass |
| Particulate Release | The average count of particulates released by a product shall not exceed 100 per milliliter greater than 5.0 microns and shall not exceed 5 per milliliter greater than 25 microns. | Pass |

<table>
<tr><th>Test Procedure</th><th>Acceptance Criteria</th><th>Result</th></tr>
<tr><td>Endotoxin</td><td>The finished devices shall not have an endotoxin level above 0.5 EU/ml for FDA and 20.0 EU/device per USP.</td><td>Pass</td></tr>
<tr><td>ETO Residual Content</td><td>The maximum residual allowed shall not exceed the allowable limits per ISO 10993-7.<br>The maximum residual allowed shall not exceed 25 ppm per Japan Notification No. 353.<br><br><table><tr><td></td><td colspan="2">Permanent Contact Devices<br>> 30 days to life</td></tr><tr><td></td><td>ETO</td><td>ECH</td></tr><tr><td>Average Daily Dose</td><td>0.1 mg/day</td><td>0.4 mg/day</td></tr><tr><td>First 24 hours</td><td>4 mg</td><td>9 mg</td></tr><tr><td>First 30 days</td><td>60 mg</td><td>60 mg</td></tr><tr><td>Lifetime</td><td>2.5 g</td><td>10 g</td></tr></table></td><td>Pass</td></tr>
<tr><td>Bioburden</td><td>The finished product shall have no more than 100 colony forming units per device.</td><td>Pass</td></tr>
<tr><td>Packaging Sterile Shelf Life</td><td>The peel test samples shall pass the peel test requirement with the peel strength of at least 1.0 lb and the bubble test samples shall pass the bubble test with no leakage per ASTM F2096-2004.</td><td>Pass</td></tr>
<tr><td>Packaging Shipping Test</td><td>All tray samples shall meet the visual inspection requirement per ASTM F1886-2004, and the tray samples shall have a seal width of 3/16-inch minimum for Lead and Pacer trays, and 5/16-inch minimum for ICD trays. All tray samples shall not exhibit any indication of seal delamination, tears, splits, opening or any indication of physical damage.</td><td>Pass</td></tr>
<tr><td>Packaging Humidity Test</td><td>All samples will be visually inspected with unaided eyes. All marking or printed information shall remain clearly legible, the adhesive fixing on the label shall not have loosened, and the label shall not become curled at any edge.</td><td>Pass</td></tr>
<tr><td>Manual and Specifications</td><td>The label and manual documents shall meet the applicable requirements of the design inputs per 60061449.</td><td>Pass</td></tr>
</table>

| Test Procedure | Acceptance Criteria | Result |
|---|---|---|
| Lead Labeling | The sample shall be visibly marked with the manufacturer, model designation, and serial number. | Pass |
| MR Conditional Identification | The sample shall have a radio opaque marker (Platinum Marker Band) that identifies it as a MR conditional lead. | Pass |
| Thermal Fatigue Preconditioning | There is no acceptance criterion as this is a preconditioning test. | Pass |
| MRI Lead Heating | For the labeled scan restrictions and after a 30 minute scan duration:<br>• The 90th percentile heating is ≤ 43 °C for myocardial tissue<br>• The 99th percentile heating is ≤ 45 °C for myocardial tissue<br>• The 99.9th percentile heating is ≤ 50 °C for blood<br>• The 99th percentile heating is ≤ 44 °C for pocket tissue, assuming a starting temperature of 35 °C | Pass |
| Static Magnetic Force | For a 1.5T MRI scanner with a maximum spatial gradient up to 19T/m, the maximum angular deflection of the lead from vertical position shall be less than or equal to 45°. | Pass |

All of the above referenced mechanical and electrical verification tests were successfully completed to demonstrate that the Tendril MRI lead met its requirements.

**Steroid Verification**

The steroid used on the Tendril MRI lead is dexamethasone sodium phosphate (DSP) and is incorporated into a monolithic controlled release device (MCRD) similar to legacy SJM leads. A complete Chemistry, Manufacturing, and Controls (CMC) section for the MCRD component and finished lead which included information and verification on product development, physical and chemical characterization, components and composition, manufacturing processes and control, finished product specifications, packaging, and stability was completed. Conditions of Approval were identified to provide additional data supporting the steroid and to expand the shelf life. The verification testing and benefit/risk assessment demonstrate that the drug component of the Tendril MRI lead is qualified as safe and effective.

**Bench Testing (outside MRI Environment) - MRI Activator**

**Sterilization**

The MRI Activator is a non-sterile product.

**Mechanical and Electrical Verification**
The MRI Activator uses a similar hardware platform as the cleared Confirm Activator (K122161). Mechanical Verification testing included: visual inspection, physical attributes, storage temperature and humidity test, and operational and humidity test. Functional Verification testing included: functional test, MRI environment functional test, and telemetry distance test and EMC/EMI testing.

**System Validation**
System validation testing was completed and included the following:

- Simulated use testing that included clinically relevant scenarios focusing on the use of the system with an emphasis on patient safety, proper functionality of the feature set, consistency of data, and performance of the system.
- MR safety testing which includes MRI in-field testing of the system including RF heating, gradient heating, vibration, injected gradient rectification, injected RF rectification, and combined field testing.

The system validation testing demonstrates that the software and firmware of the Assurity MRI/Endurity MRI meet their requirements, are validated for human use, and are safe and effective.

## B. Animal Studies

A GLP animal study (Study 628) was conducted to evaluate the electrical, mechanical, and histopathological performance of the MRI System, including the Accent MRI device (PM2218) and the Tendril MRI lead for a period of up to 26 weeks, including undergoing magnetic resonance imaging (MRI). The MRI filter in the Assurity MRI and Endurity MRI pacemakers is identical to the Accent MRI therefore this GLP demonstrates that the MRI filter is effective in the MRI environment and also that it does not interfere with the therapy functions of the device in normal operation. The animal study was conducted in compliance with applicable requirements in the Good Laboratory Practice regulations in 21CFR Part 58. The 26-weeks post implant with 1 month post MRI scan data final GLP Study 628 was analyzed. The results documented in the final report established that the Accent MRI Model PM2218 pacemaker and Tendril MRI lead Model LPA1200M implanted in this canine study demonstrated satisfactory safety and performance data.

# XI. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the use of the Accent MRI™ Pacemaker and Tendril MRI™ Lead for treatment of the conditions listed in Section II (above) in the US under IDE G100096. Data from this clinical study were the basis for the PMA approval decision for the Assurity MRI and Endurity MRI devices. The Accent MRI pacemaker was not pursued for approval but instead next generation version Assurity MRI and Endurity MRI pacemakers were approved. The Assurity MRI and Endurity MRI pacemakers utilize a

MRI filter and MRI settings which are identical to the MRI filter and parameter set incorporated in the Accent MRI pacemakers. In addition, all other device components which could have an impact on compatibility with the magnetic resonance environment are unchanged from the Accent MRI pacemaker, therefore all Accent MRI endpoint data collected during the study that provided reasonable assurance of safety and effectiveness within and outside of an MRI environment is applicable to the Assurity MRI and Endurity MRI devices.A summary of the clinical study is presented below.

## A. Study Design

Patients were treated between March 30, 2012 and October 30, 2014. The database for this PMA reflected data collected through October 30, 2014 and included 920 patients. There were 68 investigational sites.

**Study Scope, Design, and Methods**

The MRI study was a prospective, multicenter clinical investigation, consisting of a Lead Safety Phase and an MRI Phase, designed to evaluate the safety and effectiveness of the Accent MRI™ Pacemaker system indicated for implant of a pacemaker within and outside of the MRI environment. The products being evaluated were the Accent MRI pacemaker, Tendril™ MRI lead, and MRI Activator. **Figure 1:** Depicts the Lead Safety Phase of the MRI Study and **Figure 2:** Depicts the MRI Phase.

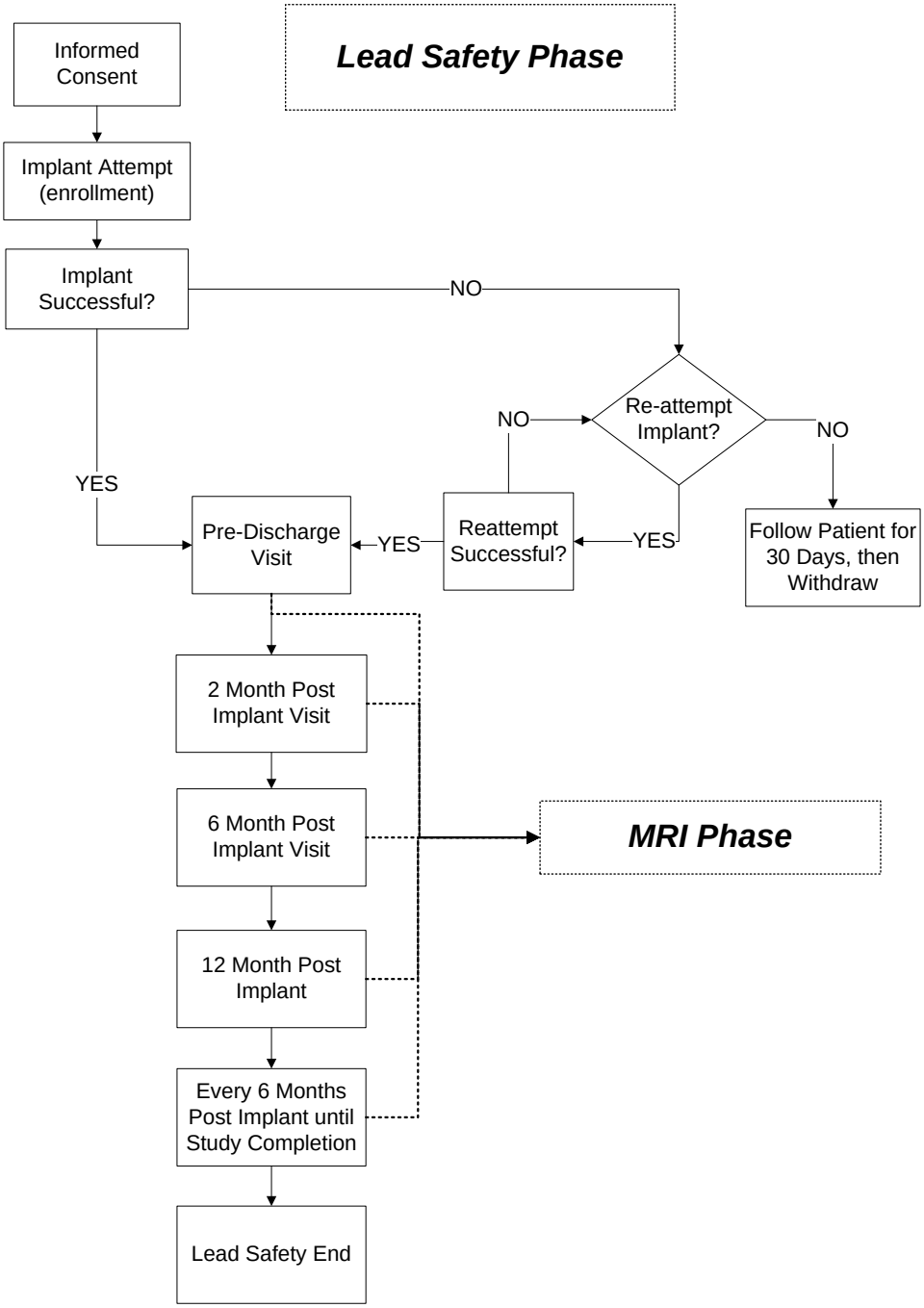


**Figure 1. MRI Study Design: Lead Safety Phase**

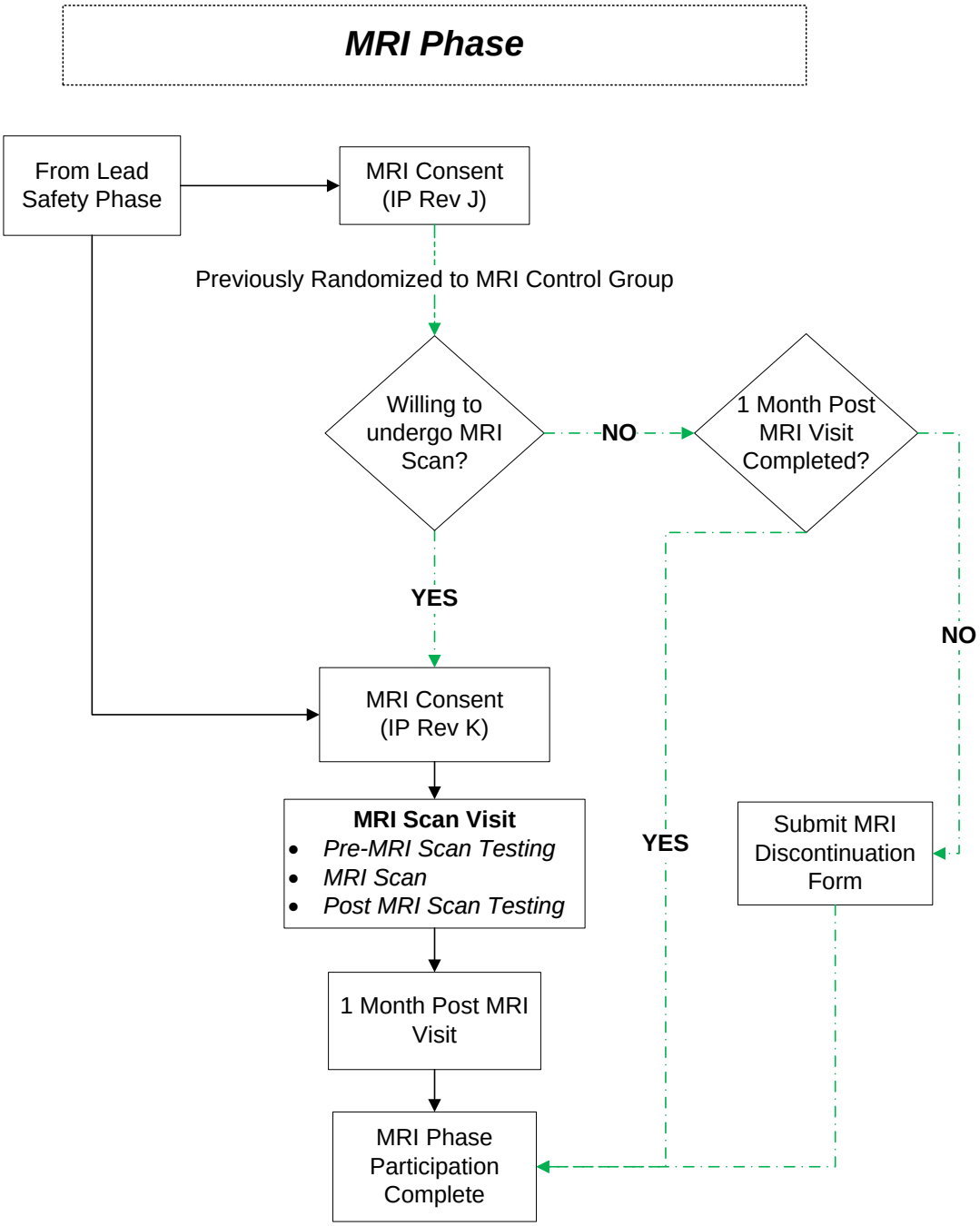


**Figure 2: MRI Study Design: MRI Phase**

An independent, unblinded Data Safety Monitioring Board (DSMB) was established to review safety data. The DSMB consisted of at least three (3) members with study-related backgrounds. Members included at least one statistician, one cardiologist, and one radiologist or cardiologist with MRI experience. A Mortality Committee also

was assembled to review and classify all patients deaths.

1. Clinical Inclusion and Exclusion Criteria
   Enrollment in the MRI study was limited to patients who met the following inclusion criteria:

   **INCLUSION CRITERIA**
   Eligible patients will met all of the following:
   - Have an approved indication per ACC/AHA/HRS guidelines for implantation of a pacemaker.
   - Will receive a new pacemaker and lead.
   - Be willing to undergo an elective MRI scan without sedation.
   - Be able to provide informed consent for study participation (legal guardian is NOT acceptable).
   - Be willing and able to comply with the prescribed follow-up tests and schedule of evaluations.
   - *Is not contraindicated for an MRI scan (per the pre-MRI safety screening form).

   Patients were not permitted to enroll in the MRI study if they met any of the following exclusion criteria:

   **EXCLUSION CRITERIA**
   Patients were excluded if they met any of the following:
   - Have an existing pacemaker or ICD. A new pacemaker and lead is required for enrollment.
   - *Have an existing active implanted medical device, e.g., neurostimulator, infusion pump, etc.
   - *Have a non-MRI compatible device or material implanted (e.g., intracranial aneurysm clip, non-MRI compatible devices or material, metals or alloys, etc.)
   - Have a lead extender or adaptor.
   - Be unable to fit in MRI bore; will come into contact with the magnet façade inside the MRI bore.
   - Have a prosthetic tricuspid heart valve.
   - Are currently participating in a clinical investigation that includes an active treatment arm.
   - Are allergic to dexamethasone sodium phosphate (DSP).
   - Are pregnant or planning to become pregnant during the duration of the study.
   - Have a life expectancy of less than 12 months due to any condition.
   - Patients with exclusion criteria required by local law (e.g., age).
   - Are unable to comply with the follow up schedule.

*Applies only to those patients who will participate in the MRI Phase of the study.

2. Follow-up Schedule

Figure 1 and Figure 2 above detail the follow up schedule for each of the study phases. Adverse events and complications were recorded at all visits.

The key timepoints are described below summarizing safety and effectiveness.

3. Clinical Endpoints

**Study Objective**
The objective of this clinical study was to verify the safety and effectiveness of the Accent MRI™ Pacemaker system indicated for implant of a pacemaker within and outside of the MRI environment.

**Primary Endpoints**
With regards to safety and effectiveness, the following are the primary endpoints defined for this study.

Lead Safety:
Safety of the Tendril MRI™ lead was evaluated in terms of freedom from Right Atrial (RA) and Right Ventricular (RV) lead-related complications for the acute (implant to 2 month visit) and chronic (2 month visit through the 12 month visit) timeframes.

MRI Safety:
The safety of the Accent MRI system was evaluated in terms of freedom from MRI scan related complications in the month following the MRI scan.

Lead Effectiveness:
Effectiveness of the Tendril MRI™ lead in was evaluated in terms of the change in bipolar atrial and ventricular capture and sensing thresholds before and after the MRI scan.

**Secondary Endpoints**
With regards to safety and effectiveness, the following are the secondary endpoints defined for this study.

Safety:
Safety of the Accent MRI™ system was evaluated in terms of freedom from system-related complications through the 12 month visit.

Effectiveness:
Effectiveness of the Tendril MRI™ lead was evaluated in terms of the bipolar atrial and ventricular capture thresholds at the MRI Visit.

## B. Accountability of PMA Cohort

At the time of database lock on October 30, 2014, 920 patients were enrolled at 68 clinical sites in the Lead Safety Phase of the Accent MRI™ Pacemaker and Tendril MRI™ Lead Investigational Device Exemption Study. The first Accent MRI PM2218 pacemaker and Tendril MRI LPA1200M leads were implanted on March 30, 2012.

Of the 920 patients enrolled in the MRI Study, 918 were successfully implanted with an Accent MRI Pacemaker system. Two (2) implants were unsuccessful due to an inability to implant the Tendril MRI lead due to difficulty in obtaining access in one patient, and a persistent left superior vena cava (SVC) in the other patient. Both patients received a market-released pacemaker system, followed for 30 days for safety after the study implant attempt, and then were withdrawn from the study per protocol.

Two hundred twenty-five (225) patients were enrolled in the MRI Phase of the MRI Study in the United States. An additional 30 supplemental scans were performed in Australia, for a total of 255 patients who contributed data to the MRI Phase. The first MRI scan was performed on April 2, 2014.

**Figure 3:** Displays the leads used and the number of successful system implants in the MRI Study. **Figure 4:** Displays the number of patients who received an MRI scan.

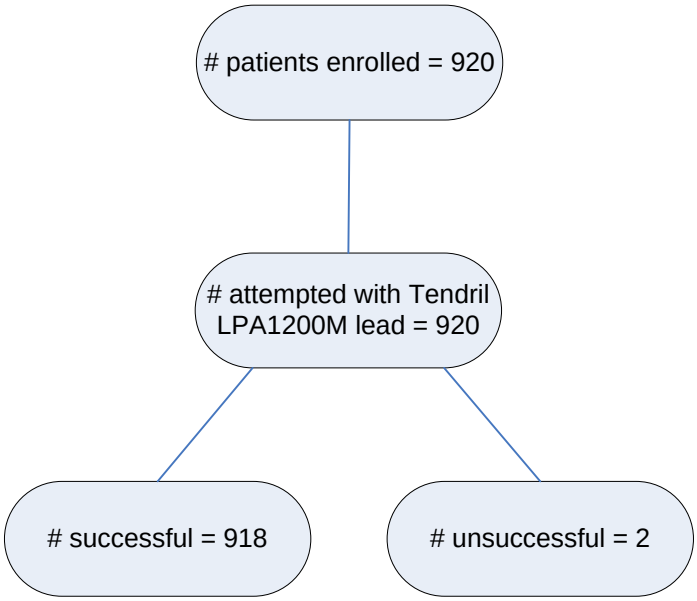


**Figure 3: Number of Patients Attempted and Implanted with the Accent MRI Pacemaker and Tendril MRI Lead**

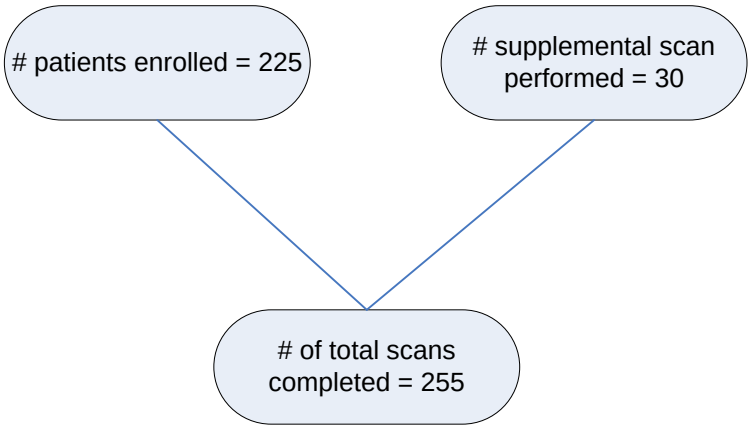


**Figure 4: Number of Patients Participating in MRI Phase/Contributing Scan Data**

As of October 30, 2014, the total time of follow up from the time of successful implant was 18,425 patient-months. The average time of follow-up was 20.00 ± 4.66 (range 0.09 to 30.68) patient-months.

As part of the Lead Safety Phase of the MRI Study, patients who were successfully implanted with the Accent MRI pacemaker system were seen at a pre-discharge during which the following tests/assessments were performed: electrical

measurements on the RA and/or RV leads and identification of the radiopaque markers on the lead and pacemaker. Patients were again seen at 2 months post implant, 6 months post implant, 12 months post implant, and every 6 months thereafter, during which the following tests/assessments were performed: electrical measurements on the RA and/or RV leads. Patients were also assessed for adverse events at all study visits.

For the MRI Phase of the study, patients completed an MRI Visit, and returned approximately 30 days later for a 1 Month Post MRI Visit. At the MRI visit, for patients consenting to undergo an MRI scan, the following tests/assessments were performed: safety screening for the MRI scan, the study MRI scan, assessment for adverse events, including MRI scan-related adverse events, and electrical measurements on the RA and/or RV leads. At the 1 Month Post MRI visit, the following tests/assessments were performed: assessment for adverse events, including MRI scan-related adverse events, and electrical measurements on the RA and/or RV leads.

## C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an IDE pacemaker study performed in the US. Table 2 below summarizes the demographic variables reported on the 920 patients who completed the implant visit in the MRI study.

**Table 2: Summary of Demographic Variables for all Enrolled Patients**

| Demographic Variable | All Enrolled Patients (N = 920) |
|---|---|
| **Age** | |
| Mean ± SD | 73.0±10.8 |
| Range (min, max) | (27,101) |
| **Gender, n (%)** | |
| Female | 421 (45.8%) |
| Male | 499 (54.2%) |
| **Cardiovascular History, n (%)** | |
| Coronary Artery Disease | 338 (36.7%) |
| Myocardial Infarction | 119 (12.9%) |
| Unstable Angina | 73 (7.9%) |

| Demographic Variable | All Enrolled Patients (N = 920) |
|---|---|
| **Prior Cardiac Interventions, n (%)** | |
| CABG | 130 (14.1%) |
| PTCA/Stents/Atherectomy | 152 (16.5%) |
| Ablation | 100 (10.9%) |
| **Non-Ventricular Arrhythmia History, n (%)** | |
| None | 370 (40.2%) |
| AF | 481 (52.3%) |
| Paroxysmal | 316 (65.7%) |
| Permanent | 63 (13.1%) |
| Persistent | 100 (20.8%) |
| AFL | 123 (13.4%) |
| AT | 41 (4.5%) |
| SVT | 55 (6.0%) |
| **Primary Indication for Device Implant, n (%)** | |
| AV Block | 242 (26.3%) |
| Pacemaker Generator Change | 2 (0.2%) |
| Prevention/Termination of Tachyarrhythmias By Pacing | 13 (1.4%) |
| Sinus Node Dysfunction | 583 (63.4%) |
| Syncope | 60 (6.5%) |
| Other | 20 (2.2%) |

**Table 3:** Summarizes all the reported data on the 225 patients who were enrolled in the MRI Phase of the study, and the 30 patients who contributed supplemental MRI scan data.

**Table 3: Summary of Demographic Variable for All Patients Contributing Data to the MRI Phase**

| Demographic Variable | Patients Enrolled in the MRI Study (N = 225) | Patients Contributing Supplemental MRI Scan Data (N = 30) | Total (N = 255) |
|---|---|---|---|
| **Age** | | | |
| Mean ± SD | 69.8±11.6 | 73.0±5.9 | 70.2±11.1 |
| Range (min, max) | (30.0,92.0) | (59.0,81.0) | (30.0,92.0) |
| **Gender, n (%)** | | | |
| Female | 98 (43.6%) | 16 (53.3%) | 114 (44.7%) |
| Male | 127 (56.4%) | 14 (46.7%) | 141 (55.3%) |
| **Cardiovascular History, n (%)** | | | |
| Coronary Artery Disease | 26 (11.6%) | 9 (30.0%) | 35 (13.7%) |
| Myocardial Infarction | 5 (2.2%) | 0 (0.0%) | 5 (2.0%) |
| Unstable Angina | 6 (2.7%) | 0 (0.0%) | 6 (2.4%) |
| **Prior Cardiac Interventions, n (%)** | | | |
| CABG | 1 (0.4%) | 1 (3.3%) | 2 (0.8%) |
| PTCA/Stents/Atherectomy | 4 (1.8%) | 4 (13.3%) | 8 (3.1%) |
| Ablation | 33 (14.7%) | 5 (16.7%) | 38 (14.9%) |
| **Non-Ventricular Arrhythmia History, n (%)** | | | |
| None | 107 (47.6%) | 4 (13.3%) | 111 (43.5%) |
| AF | 98 (43.6%) | 20 (66.7%) | 118 (46.3%) |
| Paroxysmal | 62 (63.3%) | 17 (85.0%) | 79 (66.9%) |
| Permanent | 15 (15.3%) | 1 (5.0%) | 16 (13.6%) |
| Persistent | 21 (21.4%) | 2 (10.0%) | 23 (19.5%) |
| AFL | 33 (14.7%) | 6 (20.0%) | 39 (15.3%) |
| AT | 10 (4.4%) | 6 (20.0%) | 16 (6.3%) |
| SVT | 10 (4.4%) | 0 (0.0%) | 10 (3.9%) |
| **Primary Indication for Device Implant, n (%)** | | | |
| AV Block | 59 (26.2%) | 6 (20.0%) | 65 (25.5%) |
| Pacemaker Generator | 1 (0.4%) | 0 (0.0%) | 1 (0.4%) |

| Demographic Variable | Patients Enrolled in the MRI Study (N = 225) | Patients Contributing Supplemental MRI Scan Data (N = 30) | Total (N = 255) |
|---|---|---|---|
| Prevention/Termination of Tachyarrhythmias By Pacing | 5 (2.2%) | 0 (0.0%) | 5 (2.0%) |
| Sinus Node Dysfunction | 141 (62.7%) | 18 (60.0%) | 159 (62.4%) |
| Syncope | 15 (6.7%) | 3 (10.0%) | 18 (7.1%) |
| Other | 4 (1.8%) | 3 (10.0%) | 7 (2.7%) |

## D. Safety and Effectiveness Results

1. Safety Results

**Primary Safety Endpoint Results**

**MRI Scan-Related Complications**
One hundred eighty-one (181) patients who received a study scan were analyzed for this endpoint. No MRI scan-related complications were observed.

The proportion of patients free from MRI scan-related complications was calculated as 100% with a 95% lower confidence bound of 98.37%, which is greater than the objective performance criterion of 90%.

**RA Lead-Related Complications (Implant thru 2 Month Visit)**
Eight hundred twenty-one (821) patients who had a Tendril MRI lead attempted or successfully implanted were analyzed for this endpoint. 23 RA lead-related complications were observed.

The probability of RA lead-related complications free survival at the 2-month follow-up was calculated as 97.20% with a 95% lower confidence bound of 95.81%, which is greater than the objective performance criteria of 92%.

**RV Lead-Related Complications (Implant thru 2 Month Visit)**
Nine hundred nineteen (919) patients who had a Tendril MRI lead attempted or successfully implanted were analyzed for this endpoint. Ten (10) RV lead-related complications were observed. The endpoint was successfully met, and the null hypothesis was rejected.

The probability of RV lead-related complication free survival at the 2 Month Follow Up visit was calculated as 98.45% with a 95% lower confidence bound of 96.81%, which is greater than the objective performance criteria of 92%.

**RA Lead-Related Complications (2 Month thru 12 Month Visit)**
Eight hundred six (806) patients who had a Tendril MRI lead attempted or successfully implanted, and who were not withdrawn before the 2 Month Visit,

were analyzed for this endpoint. Six (6) RA lead-related complications were observed.

The probability of RA lead-related complication free survival at the 12 Month Follow Up visit was calculated as 98.82% with a 95% lower confidence bound of 97.04%, which is greater than the objective performance criteria of 95%.

**RV Lead-Related Complications (2 Month thru 12 Month Visit)**
Nine hundred two (9)02 patients who had a Tendril MRI lead attempted or successfully implanted, and who were not withdrawn before the 2 Month Visit, were analyzed for this endpoint. No RV lead-related complications were observed.

The probability of RV lead-related complication free survival at the 12 Month Follow Up visit was calculated as 100% with a 95% lower confidence bound of 100%, which is greater than the objective performance criteria of 95%.

**Adverse effects that occurred in the PMA clinical study:**
The Reported Adverse Events summarize the adverse events in the Accent MRI™ Pacemaker and Tendril MRI™ Lead Investigational Device Exemption Study (MRI Study). The MRI study was a prospective, multicenter clinical investigation designed to evaluate the safety and effectiveness of the Accent MRI System in a patient population indicated for implant of a pacemaker within and outside of an MRI environment.

Per the investigational plan, an adverse event was defined as any unfavorable clinical event which impacts, or has the potential to impact, the health or safety of a patient caused by or associated with a study device or intervention.

Adverse events were classified as complications or observations based on the following definitions:

- Complications are defined as adverse events that require invasive intervention (e.g. lead dislodgment requiring repositioning).
- Observations are defined as adverse events that can be managed without invasive intervention (e.g., oversensing or loss of pacing capture, which is remedied by reprogramming of the pacemaker).
- Other Reported Events are any other clinical event that is submitted by the investigator which is not caused by or associated with the study device and/or system component(s) and/or defined as an Adverse Event.

**Reported Adverse Events**
**Table 4:** Lists the observations and complications reported from the MRI Study. A total of 168 adverse events have been reported in 139 patients, of which 68 are complications and 100 are observations. None of the adverse events were related to or caused by the study MRI scans. **Table 5** lists other related events.

**Table 4: MRI Study Adverse Events**

| Event Description | # of Patients with AEs* (n=920) | %of Patients with AEs | # AEs | AE/pt-years (n= 1,535.44 yrs) |
|---|---|---|---|---|
| **Complications (total)** | 63 | 6.85% | 68 | 0.044 |
| Bleeding/Hematoma | 2 | 0.22% | 2 | 0.001 |
| Cardiac Perforation | 2 | 0.22% | 2 | 0.001 |
| Cardiac Tamponade | 3 | 0.33% | 3 | 0.002 |
| Decompensated HF | 1 | 0.11% | 1 | 0.001 |
| Device Connectivity Issue | 1 | 0.11% | 1 | 0.001 |
| Device Migration | 1 | 0.11% | 1 | 0.001 |
| Elevated Pacing Thresholds - RA Lead | 2 | 0.22% | 2 | 0.001 |
| Elevated Pacing Thresholds - RV Lead | 1 | 0.11% | 1 | 0.001 |
| Hemoptysis | 1 | 0.11% | 1 | 0.001 |
| Hemothorax | 1 | 0.11% | 1 | 0.001 |
| Infection | 5 | 0.54% | 5 | 0.003 |
| Lead dislodgement or migration - RA Lead | 24 | 2.61% | 25 | 0.016 |
| Lead dislodgement or migration - RV Lead | 7 | 0.76% | 7 | 0.005 |
| Lead fracture | 1 | 0.11% | 1 | 0.001 |
| Pacemaker Induced Cardiomyopathy | 1 | 0.11% | 1 | 0.001 |
| Pericardial effusion | 2 | 0.22% | 2 | 0.001 |
| Phrenic nerve/diaphragmatic stimulation | 1 | 0.11% | 1 | 0.001 |
| Pneumothorax | 4 | 0.43% | 4 | 0.003 |
| Pocket site/incision pain lasting greater than 72 hours post implant | 2 | 0.22% | 2 | 0.001 |
| Stenosis of the left subclavian vein | 1 | 0.11% | 1 | 0.001 |

| Event Description | # of Patients with AEs* (n=920) | %of Patients with AEs | # AEs | AE/pt-years (n= 1,535.44 yrs) |
|---|---|---|---|---|
| Thrombo-embolic event | 1 | 0.11% | 1 | 0.001 |
| Twiddler's Syndrome | 1 | 0.11% | 1 | 0.001 |
| Undersensing - RA Lead | 1 | 0.11% | 1 | 0.001 |
| Wound dehiscence | 1 | 0.11% | 1 | 0.001 |
| **Observations (total)** | 87 | 9.46% | 100 | 0.065 |
| Atrial Arrhythmia | 3 | 0.33% | 3 | 0.002 |
| Bleeding/Hematoma | 9 | 0.98% | 9 | 0.006 |
| Cellulitis/thrombophlebitis | 1 | 0.11% | 1 | 0.001 |
| Cerebrovascular accident | 1 | 0.11% | 1 | 0.001 |
| Decompensated HF | 2 | 0.22% | 2 | 0.001 |
| Elevated pacing thresholds – RA Lead | 3 | 0.33% | 3 | 0.002 |
| Elevated pacing thresholds – RV Lead | 1 | 0.11% | 1 | 0.001 |
| Excessive rate responsive pacing | 1 | 0.11% | 1 | 0.001 |
| Extracardiac stimulation | 1 | 0.11% | 1 | 0.001 |
| Infection | 4 | 0.43% | 4 | 0.003 |
| Lead dislodgement or migration - RA Lead | 3 | 0.33% | 3 | 0.002 |
| Lead dislodgement or migration - RV Lead | 1 | 0.11% | 1 | 0.001 |
| Loss of Capture - RA Lead | 1 | 0.11% | 1 | 0.001 |
| Loss of Capture - RV Lead | 1 | 0.11% | 1 | 0.001 |
| Mechanical abnormality of pacemaker pocket | 1 | 0.11% | 1 | 0.001 |
| Noise reversion | 2 | 0.22% | 2 | 0.001 |

| Event Description | # of Patients with AEs* (n=920) | %of Patients with AEs | # AEs | AE/pt-years (n= 1,535.44 yrs) |
|---|---|---|---|---|
| Oozing from implant site | 1 | 0.11% | 1 | 0.001 |
| Oversensing - RA Lead | 2 | 0.22% | 2 | 0.001 |
| Pacemaker mediated tachycardia (PMT) | 20 | 2.17% | 21 | 0.014 |
| Pain at device site | 1 | 0.11% | 1 | 0.001 |
| Pectoral stimulation | 1 | 0.11% | 1 | 0.001 |
| Pericardial effusion | 4 | 0.43% | 4 | 0.003 |
| Pericarditis | 3 | 0.33% | 3 | 0.002 |
| Phrenic nerve/diaphragmatic stimulation | 1 | 0.11% | 1 | 0.001 |
| Pleural effusion | 1 | 0.11% | 1 | 0.001 |
| Pneumothorax | 7 | 0.76% | 7 | 0.005 |
| Pocket site/incision pain lasting greater than 72 hours post implant | 5 | 0.54% | 5 | 0.003 |
| Repetitive Nonreentrant Ventriculoatrial Synchrony | 1 | 0.11% | 2 | 0.001 |
| Set screw damage | 1 | 0.11% | 1 | 0.001 |
| Tachycardia | 1 | 0.11% | 1 | 0.001 |
| Thrombo-embolic event | 9 | 0.98% | 9 | 0.006 |
| Undersensing - RA Lead | 2 | 0.22% | 2 | 0.001 |
| Undersensing - RV Lead | 2 | 0.22% | 2 | 0.001 |
| Undersensing - PG | 1 | 0.11% | 1 | 0.001 |

* Some patients experienced more than one event and therefore the number of patients is less than the number of events.

**Table 5: MRI Study Other Reported Events**

| Other Reported Events Description | # of Patients | # of Events | Comments |
|---|---|---|---|
| Acute Encephalopathy | 1 | 1 | Hospitalized for general weakness, altered mental status and mild CHF. |
| Angina | 6 | 7 | Patients hospitalized for chest pain; angioplasty performed in one patient, angioplasty and stenting performed in one patient and stent placed in one patient. No action taken in one patient. |
| Aortic Valve Replacement | 1 | 1 | Patient had history of aortic stenosis; valve replaced with no sequelae. |
| Arrest – Cardiopulmonary | 1 | 1 | Patient brought to ER in full arrest; cardioverted and intubated. Patient ultimately expired. |
| Arrest – Respiratory | 1 | 2 | Patient aspirated on an ice chip and went into respiratory failure ultimately resulting in patient death. |
| Asystole | 1 | 1 | Patient suffered an acute MI at home and expired |
| Atrial Arrhythmia | 24 | 26 | Patients had chronic atrial arrhythmias prior to device implant or arrhythmias were not attributed to the study device/procedure. |
| Atrial Fibrillation | 2 | 2 | Medication adjusted in one patient; catheter ablation done in one patient. |
| Atrial Flutter | 1 | 1 | Medication adjusted |
| Cerebrovascular Accident (CVA) | 5 | 5 | The CVA remained unresolved in four patients, two (2) of whom died as a result of the CVA. One patient went through rehabilitation and recovered. |
| Chest Pain | 5 | 5 | Chest pain resolved with no action in three patients. Medication was adjusted on two (2) patients one of which had cardiac catheterization. |
| Compression Fracture L2 Vertebral Body | 1 | 1 | Patient treated with Kyphoplasty |
| Decompensated Heart Failure | 9 | 9 | Medications added or adjusted. One patient died due to multiple comorbidities. |
| Device Upgraded to CRT | 1 | 1 | Tendril MRI RA lead retained. Patient remains active in study. |

| Other Reported Events Description | # of Patients | # of Events | Comments |
|---|---|---|---|
| Electromagnetic Interference | 1 | 1 | Event unresolvable; no action was taken. |
| Elevated Pacing Thresholds | 1 | 2 | Events occurred during initial lead placement; resolved once final lead placement was obtained. |
| Episodic Dizziness | 1 | 1 | Event resolved with medications adjustment. |
| Fall | 2 | 2 | Falls unrelated to device or cardiac issues. |
| Gastroenteritis | 1 | 1 | Patient treated with medication; no additional sequelae. |
| Hypotension | 2 | 2 | Medications adjusted; no additional sequelae observed. |
| Left Arm Swelling | 1 | 1 | No DVT; no action required. |
| Left Shoulder Pain | 1 | 1 | Pain unrelated to device/implant; no action required. |
| Lumbar Spinal Stenosis | 2 | 2 | Patients surgically treated; unrelated to device/study procedures. |
| Mitral Stenosis | 1 | 1 | MVR with single vessel coronary artery bypass grafting (CABG). |
| Nausea & Generalized Weakness | 1 | 1 | Patient withdrew from study due to other underlying medical conditions unrelated to study device/procedures. |
| Perforated Appendix With Abscess | 1 | 1 | Patient had laparoscopic appendectomy. |
| Pericardial Effusion | 1 | 1 | Effusion occurred five months post system implant; determined to be unrelated to study system or procedure. |
| Pleural Effusion | 1 | 1 | Patent underwent right thoracentesis. |
| Pulmonary Edema | 1 | 1 | Noted on chest x-ray; no intervention required. |
| Shock/Hypotension | 2 | 2 | One patient treated with medication; one patient expired; death unrelated to device/study procedures. |
| Shortness of Breath | 2 | 2 | Device was reprogrammed in one patient. No action taken the other patient. |
| Syncope | 2 | 2 | Device reprogrammed |

| Other Reported Events Description | # of Patients | # of Events | Comments |
|---|---|---|---|
| Thrombocytopenia | 1 | 1 | Unresolvable; multiple comorbidities |
| Thrombo-embolic Event | 2 | 2 | Patients treated with anticoagulants |
| Ventricular Arrhythmia | 9 | 10 | One patient died; the death was adjudicated as not related to study device/procedure. |
| Ventricular Tachycardia | 1 | 1 | No intervention required |
| **Total** | **78**** | **103** | **-** |

** Some patients experienced more than one event and therefore the number of patients is less than the number of events.

**Death Summary**

Fifty-six (56) patients enrolled in the MRI study were withdrawn from the study due to death. Three (3) of the deaths were considered to be *peri-operative mortalities* (occurred ≤ 30 days post-implant). There were no deaths classified as related to the pacemaker or lead system and there were no deaths classified as related to the MRI procedure.

**Table 6: Events Committee Classification of Paitent Deaths**

| Primary Cause | Number of Patients |
|---|---|
| Cardiac: Arrhythmic | 4 |
| Cardiac: Ischemic | 1 |
| Cardiac: Pump Failure | 4 |
| Cardiac: Unknown | 1 |
| Non-Cardiac | 40 |
| Unknown | 6 |
| TOTAL | 56 |

2. Effectiveness Results

**Primary Effectiveness Endpoint Results**

**MRI RA Lead Capture Threshold Effectiveness**

One hundred forty-four (144) patients who were implanted with an RA lead, received a study scan, and had capture threshold data Pre and 1 month post MRI scan were included in this analysis.

The proportion of patients who experienced a capture threshold increase of ≤0.5V at 0.5ms from before to the 1 month Post MRI visit was calculated 100% with a 95% lower confidence bound of 97.47%, which is greater than the objective performance criterion of 90%.

**MRI RV Lead Capture Threshold Effectiveness**
One hundred sixty-seven (167) patients who were implanted with an RV lead, received a study scan, and had capture threshold data Pre and 1 month post MRI scan were included in this analysis.

The proportion of patients who experienced a capture threshold increase of ≤0.5V at 0.5ms from before to the 1 month Post MRI visit was calculated 100% with a 95% lower confidence bound of 97.82%, which is greater than the objective performance criterion of 90%.

**MRI RA Lead Sensing Threshold Effectiveness**
One hundred twenty-one (121) patients who were implanted with an RA lead, received a study scan, and had sensing threshold data Pre and 1 month post MRI scan were included in this analysis.

The proportion of patients who experienced a sensing threshold decrease of ≤50% and atrial sensing amplitude at 1-month post MRI visit of ≥1.5 mV was calculated 92.56% with a 95% lower confidence bound of 86.35%, which is greater than the objective performance criterion of 85%.

**MRI RV Lead Sensing Threshold Effectiveness**
One hundred thirty-four (134) patients who were implanted with an RV lead, received a study scan, and had sensing threshold data Pre and 1 month post MRI scan were included in this analysis.

The proportion of patients who experienced a sensing threshold decrease of ≤50% and atrial sensing amplitude at 1-month post MRI visit of ≥1.5 mV was calculated 97.76% with a 95% lower confidence bound of 93.60%, which is greater than the objective performance criterion of 87%.

**Secondary End Point Results**
**System-Related Complications**
Nine hundred twenty (920) patients who had an Accent MRI pacemaker system attempted or successfully implanted were analyzed for this endpoint. Forty-five (45) system-related complications (RA lead, RV lead, Pacemaker and System-related complications) were observed.

The probability of system-related complication free survival at the 12 Month Follow Up visit was calculated as 94.64% with a 95% lower confidence bound of 92.76%, which is greater than the objective performance criterion of 80%.

**RA Lead Capture Threshold at the MRI Visit (pre-scan)**
The proportion of patients who experienced a capture threshold of ≤2.0 V at 0.5ms at the MRI visit (pre-scan) was calculated as 100% with a 95% lower confidence bound of 97.69%, which is greater than the objective performance

criterion of 85%.

**RV Lead Capture Threshold at the MRI visit (pre-scan)**
The proportion of patients who experienced a capture threshold of ≤2.0 V at 0.5ms at the MRI visit (pre-scan) was calculated as 100% with a 95% lower confidence bound of 97.98%, which is greater than the objective performance criterion of 85%.

**Patient Discontinuation/Withdrawals**
A total of 105 patients participating in MRI Study were withdrawn from the study. Two (2) patients were withdrawn approximately one month after unsuccessful system implants in accordance with the protocol. Fifty-six (56) patients died and were also withdrawn from the study. In addition to these two (2) unsuccessful implants and 56 deaths, 47 additional patients were withdrawn from the study.

**Table 7: Reasons for patient withdrawals**

| Reason for Withdrawal | Number of Patients |
|---|---|
| Patient And/Or Family Request | 27 |
| Patient Death | 56 |
| Patient Lost To Follow Up | 2 |
| Patient Participation Terminated By Investigator | 5 |
| System Explanted Without A System Replacement | 13 |
| Unsuccessful Implant | 2 |
| **Total** | **105** |

3. Subgroup Analyses
   No preoperative characteristics were evaluated for potential association with outcomes.

4. Pediatric Extrapolation
   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. **Financial Disclosure**

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included five (5) investigators of which none were full-time or part-time employees of the sponsor and five (5) had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0 of investigators.
- Significant payment of other sorts: 5 of investigators.
- Proprietary interest in the product tested held by the investigator: 0 of investigators.
- Significant equity interest held by investigator in sponsor of covered study: 0 of investigators.

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

## XI PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

## XII CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

### A. Effectiveness Conclusions

The preclinical and clinical results demonstrate a reasonable assurance of effectiveness for the SJM Brady MRI System both within and outside of an MRI environment. Basic effectiveness of the device was demonstrated through preclinical testing. The SJM Brady MRI System clinical study demonstrated that the system continues to function appropriately and without adverse consequences for patients when exposed to the MRI environment under the specified MRI conditions of use.

### B. Safety Conclusions

The risks of the SJM Brady MRI System are based on data collected in a clinical study conducted to support PMA approval. The preclinical and clinical results demonstrate a

reasonable assurance of safety for the SJM Brady MRI System both within and outside of an MRI environment.

### C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The primary benefit of the MR conditional pacing system is that it provides patients with the option to undergo a MRI scan when clinically necessary, while defining the conditions for use that maximize patient safety. In patients with permanent pacemakers, MRI may provide important diagnostic benefits, since this technique has advantages over other imaging modalities. The importance and utilization of MRI technology is increasing and the number of MRI scans continues to rise. This rising trend is expected to continue in the years to come which further stress the importance of providing the physician with the option to utilize a MR Conditional Pacing System.

Patient Perspectives: This submission did not include specific information on patient perspective for this device.

In conclusion, given the available information above, the data support that for the MR Conditional Pacing System the probable benefits outweigh the probable risks.

### D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The SJM Brady MRI System was designed to enable patients to undergo MRI scans under specified conditions. Preclinical testing was completed to evaluate the safety and effectiveness of the device within and outside an MRI environment. Clinical testing performed under an IDE further evaluated the system and confirmed the safety profile of the system is similar to other pacemaker systems. The preclinical and clinical data provide a reasonable assurance that the St. Jude Medical MR Conditional Pacemaker System is safe and effective.

## XIII CDRH DECISION

CDRH issued an approval order on January 31, 2017. The final conditions of approval cited in the approval order are described below.

Non-Clinical Steroid Conditions of Approval

FDA notes that you have made efforts to improve the manufacturing controls of the drug components of the subject leads. However, FDA identified several items that require further updates and improvement. These items are outlined in detail below as non-clinical conditions of approval. To satisfy these conditions of approval you will need to address each item.

FDA is allowing this information to be submitted as a post-approval commitment based upon the unique collection of evidence submitted under this PMA. Future submissions should meet all premarket requirements for the drug component as requested in the PMA

submission. Within 30 days, please provide a timeline for your proposal to address these items. For any item below not addressed within 6 months of approval, you will be required to provide interim reporting every 6 months on the progress made with respect to addressing the below items until a PMA/S is submitted as necessary to remove the below conditions.

1. You should collect release and stability data for 3 batches of finished product made with the final manufacturing controls and test methods and provide the data to FDA to support the regulatory specification and a shelf life for the LPA1200M finished lead. As described in your commitment stability study protocol 60074333, please use the same 3 finished product batches for long-term, intermediate (if warranted), and accelerated stability studies to support an expiration date.

   For 3 batches of finished leads manufactured according to the commercial process (with all process revisions and optimizations), provide:

   a. By Q3 CY2017 (or Within 6 months of PMA approval), provide an initial report with release data and 6 months of long-term and all available accelerated stability data
   b. By Q1 CY2018 (or Within 12 months of PMA approval), provide a second report with 12 months of long-term and 6 months of accelerated stability data

2. By Q4 CY2017 (or within 9 months of PMA approval), submit updated acceptance criteria for your drug elution test method and submit an updated Regulatory Specification Table reflecting the updated criteria. Your criteria should take into account the following:

   a. Elution data from the stability batches of final finished leads manufactured with all the improved processes must be used.
   b. In general, the selection of the drug elution acceptance criteria ranges is based on mean target value ±10% and NLT 80% for the last sampling time-point. However, if the drug elution plateau does not reach 80%, the limit for the last time point should be adjusted as appropriate.
   c. The drug elution acceptance criteria should be set in a way to ensure consistent performance from lot to lot.

3. By Q3 CY2017 (or within 6 months of PMA approval), provide long-term stability data (including elution) for the MCRD component using the improved manufacturing process to support an in-process hold time of longer than 4 months. Such data will include finished product release data from leads built using MCRDs that have been stored in inventory for the maximum hold time to support the finished lead continuous flow manufacturing approach.

a. Since in-process components should have tighter quality controls to ensure that the finished lead will meet the regulatory specification at release throughout shelf-life, the proposed impurity limits for the MCRD component should be tightened (i.e., dexamethasone NMT 2.0% and total impurities NMT 5.0%).

4. By Q1 CY2018 (or within 12 months of PMA approval), complete a bridging study using a minimum of 3 batches of MCRDs (or distal tip subassemblies) and 3 batches of finished leads manufactured using the proposed improved processes and analytical procedures to provide support for using MCRD component (or distal tip subassembly) testing in lieu of testing the proposed commercial product LPA1200M lead. The bridging study may evaluate the following drug attributes: assay, identity, content uniformity, impurities/degradants, and elution. Please indicate the batch numbers of the MCRD components (or distal tip subassemblies) and finished leads used in the study.

5. By Q3 CY2017 (or within 6 months of PMA approval), submit your proposal for the assignment of the part and batch numbers.

6. Please note that the interim shelf life of the finished lead cannot be extended beyond that given at commercial approval until you have fulfilled commitments #1 and 2 listed above.

Post Approval Study Conditions of Approval

OSB Lead PMA Post-Approval Study – SJM Brady MRI Post Approval Study. The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. This study will be conducted as per protocol dated November 30, 2015 included in P140033/A006. The purpose of this study is to evaluate the long term safety of Tendril MRI lead implanted with a SJM Brady MRI implantable pulse generator (IPG) in subjects with a standard bradycardia pacing indication and the safety of the pacemaker system in an MRI environment. This is a prospective, multi-center clinical study designed to evaluate the long-term safety of the Tendril MRI lead implanted with a SJM Brady MRI IPG in subjects with a standard bradycardia pacing indication. The primary hypothesis is to demonstrate that the complication-free probability is greater than 92.5% at five years post-implant for Tendril MRI right atrial (RA) lead and Tendril MRI right ventricular (RV) lead. The minimum enrollment requirement for completing this study is 1756 subjects including Accent MRI IDE study roll over subjects at up to 70 centers in (>50%) and outside of the US. Primary endpoints are to assess Tendril MRI RA/VA lead-related complications through 60 months of follow up and MRI scan-related complications rate through one-month following the MRI scan. The MRI scan-related complication rate will be presented as the probability of an occurrence of MRI Scan related complications. The study will evaluate long-term lead safety of the Tendril MRI lead at 60 months with study evaluations occurring every six (6) months following enrollment.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

## XIV APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.